REMARKS/ARGUMENTS

Claim 21 is active and new Claims 45-47 have been added. Claims 43-44 have been withdrawn from consideration. Independent Claims 21, 43 and 44 have been revised to refer to three specific types of fusion proteins consistent with their previous elections of species. The specific fusion protein determinants are also described on page 19 of the specification and the fluorescent proteins on page 21, lines 7 *ff.* New Claims 45-47 track Claims 21, 43 and 44 but encompass cells which may express additional fusion proteins besides those specifically recited. Cells expressing more than three different fusion proteins are described at the bottom of page 18 of the specification. Accordingly, the Applicants do not believe that any new matter has been added.

Election/Restriction

The Applicants previously elected Group I, Claims 1-10, directed to cell-division visualized cells containing three or more genes encoding fluorescent fusion proteins. As species of fusion proteins, the Applicants previously elected histone H3 (a nucleus/chromosome protein) and importin α (a nuclear membrane protein). The current claims are directed to cells containing histone H3-CFP, Importin α-DsRed and α-tubulin-GFP.

Claims 43-44 have been withdrawn from consideration and track non-elected Groups II and III. In the event that this restriction requirement is maintained, the Applicants respectfully request that the claims of the nonelected group(s) which depend from or otherwise include all the limitations of an allowed elected claim, be rejoined upon an indication of allowability for the elected claim, see MPEP 821.04.

Rejection—35 U.S.C. §103

Claims 21-23, 25, 27, 41 and 42 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al., Nature Cell. Biol. 13:852, in view of Rusan et al., Mol. Biol. Cell. 12:971. Except for Claim 21, these claims have been cancelled.

The invention is directed to a cell comprising histone H3-CFP, Importin α-DsRed and α-tubulin-GFP. Gerlich do not disclose any of these fusion proteins, but refer instead to NRK cells expressing histone H2B-cyan fluorescent protein + lamin B receptor-yellow fluorescent protein + γ-tubulin-red fluorescent protein.

Rusan is indicated as disclosing LLCPK-1α cells expressing α-tubulin-green fluorescent protein.

The cited art does not disclose all the elements of the invention, therefore, it does not render the invention obvious.

Moreover, there is no suggestion in the cited art to specifically select the three specific fusion proteins required by the invention, nor any reasonable expectation of success for the superior properties of this combination with respect to visualizing cell dynamics.

As shown in the attached Declaration of Dr. Sugimoto (see color copies), this combination of fusion proteins provides superior monitoring of spindle, nuclear envelope, and nucleus/chromosomal dynamics from prophase to telophase. The properties of the claimed combination in comparison to a combination where α-tubulin is replaced by a different protein, Aurora A-GFP, are partially summarized in the table below.

	Experiment 1	Experiment 2
Fusion proteins that the cells express:	**α-tubulin GFP (green)**	**Aurora A-GFP (green)**
	H3-CFP (cyan)	H3-CFP (cyan)
	DsRed-Importin-α (red)	DsRed-Importin-α (red)
Results:		Does not show the structure of mitotic spindle through process of cell division.

		MTOCs (microtubules organizing centers) and aster unclear by comparison to Experiment 1 (Fig. 1)
		Appearance of mitotic spindles unclear in metaphase to telophase (E-H} compared to Experimental 1 (Fig. 1).

Therefore, the Applicants respectfully request that this rejection be withdrawn since the prior art does not disclose or suggest all the elements of the invention, nor provide any reasonable expectation of success for the superior properties of the combination required by the present claims.

Rejection—35 U.S.C. §103

Claims 21-25, 27, 41 and 42 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al., Nature Cell. Biol. 13:852, in view of Rusan et al., Mol. Biol. Cell. 12:971, and further in view of Kimura et al., J. Cell. Biol. 153:1341. Except for Claim 21, these claims have been cancelled.

Gerlich and Rusan have been addressed above and do not disclose or suggest all the elements of the invention, nor do they provide a reasonable expectation of success for the superior properties provided by this combination.

Kimura was cited as disclosing the substitution of histone-H2B with histone H3 in fusion proteins with green fluorescent protein (GFP). However, Kimura does not disclose histone H3-CFP (cyan) or Importin α-DsRed and α-tubulin-GFP as required by the present claims. Nor does it provide a reasonable expectation of success for the superior properties provided by this combination of fusion proteins. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. §103

Claims 21-25, 27, 41 and 42 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al., Nature Cell. Biol. 13:852, in view of Rusan et al., Mol. Biol. Cell. 12:971, and further in view of Kim et al., J.B.C. 275:23139. Except for Claim 21, these claims have been cancelled.

Gerlich and Rusan have been addressed above and do not disclose or suggest all the elements of the invention, nor do they provide a reasonable expectation of success for the superior properties provided by this combination.

Kim was cited as disclosing a fusion protein comprising importin α and green fluorescent protein (GFP). However, it does not disclose Importin α-DsRed, or histone H3-CFP (cyan) and α-tubulin-GFP as required by the present claims. Nor does it provide a reasonable expectation of success for the superior properties provided by this combination of fusion proteins. Therefore, the Applicants submit that this rejection is not sustainable.

Rejection—35 U.S.C. §103

Claims 21-27, 41 and 42 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sugimoto et al., Mol. Biol. Cell 13:50a-51a, in view of Rusan et al., Mol. Biol. Cell. 12:971. Except for Claim 21, these claims have been cancelled.

Neither Sugimoto, nor Rusan disclose a cell expressing the three specific types of fusion proteins required by the present claims: α-tubulin-GFP, histone H3-CFP and Importin α-DsRed.

While Sugimoto disclose a cell expressing the combination of Aurora-A-GFP (green), histone H3-CFP (cyan) and Importin-α-DsRed, they do not suggest substituting α-tubulin-GFP for Aurora-A-GFP. Moreover, they do not provide a reasonable expectation of success that such a substitution would provide a superior ability to visualize cell dynamics.

On the other hand, as shown by the attached Declaration of Dr. Sugimoto, this specific combination of fusion proteins provides superior monitoring of spindle, nuclear envelope, and nucleus/chromosomal dynamics from prophase to telophase. These results are partially summarized in the table below.

	Experiment 1	Experiment 2
Cells express:	**α-tubulin GFP (green)**	**Aurora A-GFP (green)**
	H3-CFP (cyan)	H3-CFP (cyan)
	DsRed-Importin-α (red)	DsRed-Importin-α (red)
Results:		Does not show the structure of mitotic spindle through process of cell division.
		MTOCs (microtubules organizing centers) and aster unclear by comparison to Experiment 1 (Fig. 1)
		Appearance of mitotic spindles unclear in metaphase to telophase (E-H} compared to Experimental 1 (Fig. 1).

The rejection indicates that it would have been obvious to replace the GFP-Aurora A fusion protein of Sugimoto with an α-tubulin GFP fusion protein of Rusan. However, Rusan does not teach or suggest combination of α-tubulin-GFP with other fusion proteins, such as histone H3-CFP and Importin αDs-Red and is silent about the particular combination required by Claim 21.

Thus, neither document provides any specific reason to select α-tubulin GFP fusion protein instead of the Aurora-A GFP, nor does it provide a reasonable expectation of success for the superior results obtained by the combination of fusion proteins required by the present claims and as shown in part by the data in the attached Declaration. Therefore, the Applicants respectfully submit that this rejection is unsustainable.

CONCLUSION

In view of the amendments and remarks above, the Applicants respectfully submit that this application is now in condition for allowance. An early notice to that effect is earnestly solicited.

Respectfully submitted,

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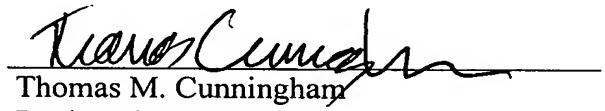
Norman F. Oblon



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